PATENT

DOCKET NO.: CHEM0005US PL/ISIS-5782 Application No.: 10/700,971

Office Action Dated: August 18, 2011

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (currently amended) A composition comprising:

a first oligonucleotide and a second oligonucleotide, wherein:

the first oligonucleotide and the second oligonucleotide are not covalently linked to each other.

at least a portion of the first oligonucleotide is complementary to at least a portion of the second oligonucleotide and to a target nucleic acid; and

at least one of the first and second oligonucleotides comprises a conjugate group;

wherein at least one of (i) the first oligonucleotide comprises a 5' region comprising 2'-OCH₃ modified nucleosides; a central region comprising b-D-ribonucleosides; and a 3' region comprising 2'-OCH3 modified nucleosides and (ii) the second oligonucleotide comprises a 5' region comprising nucleosides joined by phosphorothioate linkages; a central region comprising B-D-ribonucleosides; and a 3' region comprising nucleosides joined by phosphorothioate linkages is present.

2-3. (canceled)

(currently amended) The composition of claim 1 wherein each of the first and second 4 oligonucleotides comprises 17 to 25 nucleotides.

5-8. (canceled)

9. (currently amended) The composition of claim 1 wherein the second oligonucleotide comprises a plurality of ribose nucleotide units.

10-100. (canceled) DOCKET NO.: CHEM0005US.P1/ISIS-5782 Application No.: 10/700,971

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101. (original) A pharmaceutical composition comprising the composition of claim 1 and a pharmaceutically acceptable carrier.

102-109. (canceled)

- 110. (previously presented) The composition of claim 1 wherein the first oligonucleotide comprises
 - a 5' region comprising 2'-OCH3 modified nucleosides;
 - a central region comprising β-D-ribonucleosides; and
 - a 3' region comprising 2'-OCH3 modified nucleosides.
- 111. (previously presented) The composition of claim 110 wherein the nucleosides in the 5' and 3' regions are joined by phosphorothioate linkages.
- 112. (previously presented) The composition of claim 111 wherein the nucleosides in the central region are joined by phosphorothioate linkages.
- 113. (previously presented) The composition of claim 1 wherein the second oligonucleotide comprises
 - a 5' region comprising nucleosides joined by phosphorothioate linkages;
 - a central region comprising β-D-ribonucleosides; and
 - a 3' region comprising nucleosides joined by phosphorothioate linkages.
- 114. (previously presented) The composition of claim 113 wherein the 5' and 3' regions each independently comprise 2'-OCH₃ modified nucleosides.